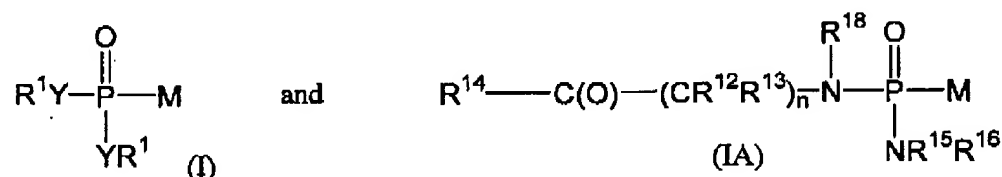


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Docket No. MET-037CXT
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1. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically effective amount of at least one insulin secretagogue and a pharmaceutically effective amount of at least one FBPase inhibitor, wherein said insulin secretagogue is selected from a group consisting of sulfonylurea antidiabetic agents and non-sulfonylurea antidiabetic agents, and the FBPase inhibitor is selected from the group consisting of formulae I and IA and pharmaceutically acceptable prodrugs and salts thereof, wherein formulae I and IA are as follows:



wherein *in vivo* or *in vitro* compounds of formulae I and IA are converted to M-PO_3^{2-} , which inhibits FBPase, and wherein:

Y is independently selected from -O- and $-\text{NR}^6$, with the provisos that:

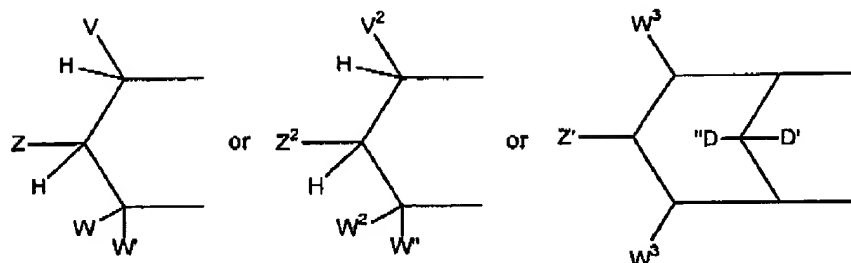
when Y is -O-, the R^1 attached to -O- is independently selected from -H, alkyl, optionally substituted aryl, optionally substituted alicyclic where the cyclic moiety contains a carbonate or a thiocarbonate, optionally substituted -arylalkyl, $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{NR}^2$, $-\text{NR}^2-\text{C}(\text{O})-\text{R}^3$, $-\text{C}(\text{R}^2)_2-\text{OC}(\text{O})\text{R}^3$, $-\text{C}(\text{R}^2)_2-\text{O}-\text{C}(\text{O})\text{OR}^3$, $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{SR}^3$, -alkyl-S-C(O) R^3 , -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y is $-\text{NR}^6$, the R^1 attached to $-\text{NR}^6$ is independently selected from -H, $-\text{C}(\text{R}^2)_2\text{COOR}^3$, $-\text{C}(\text{R}^4)_2\text{COOR}^3$, $-\text{C}(\text{R}^2)_2\text{C}(\text{O})\text{SR}$, and -cycloalkylene-COOR³, where q is 1 or 2;

when only one Y is -O-, which -O- is not part of a cyclic group containing the other Y, the other Y is $-\text{N}(\text{R}^{18})-(\text{CR}^{12}\text{R}^{13})-\text{C}(\text{O})-\text{R}^{14}$; and

when Y is independently selected from -O- and $-\text{NR}^6$, together R^1 and R^1 are alkyl-S-S-alkyl- and form a cyclic group, or together, R^1 and R^1 form:

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wherein

a) V is selected from the group of aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkynyl and 1-alkenyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V; or

Z is selected from the group of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC}(\text{O})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{OR}^3$, $-\text{CHR}^2\text{OC}(\text{O})\text{SR}^3$, $-\text{CHR}^2\text{OCO}_2\text{R}^3$, $-\text{OR}^2$, $-\text{SR}^2$, $-\text{CHR}^2\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^2_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$, $-\text{R}^2$, $-\text{NR}^2_2$, $-\text{OCOR}^3$, $-\text{OCO}_2\text{R}^3$, $-\text{SCOR}^3$, $-\text{SCO}_2\text{R}^3$, $-\text{NHCOR}^2$, $-\text{NHCO}_2\text{R}^3$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_p-\text{OR}^2$, and $-(\text{CH}_2)_p-\text{SR}^2$, where p is an integer 2 or 3; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

W and W' are independently selected from the group of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl and 1-alkynyl; or

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

b) V^2 , W^2 and W'' are independently selected from the group of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

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Z^2 is selected from the group of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC}(\text{O})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{R}^3$, $-\text{CHR}^2\text{OCO}_2\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{O})\text{SR}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{OR}^3$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^2_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2_2)\text{OH}$, $-\text{SR}^2$, $-\text{CH}_2\text{NHaryl}$, $-\text{CH}_2\text{aryl}$; or

together V^2 and Z^2 are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally containing 1 heteroatom, and substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from a Y attached to phosphorus;

c) Z' is selected from the group of $-\text{OH}$, $-\text{OC}(\text{O})\text{R}^3$, $-\text{OCO}_2\text{R}^3$, and $-\text{OC}(\text{O})\text{SR}^3$;

D' is $-\text{H}$;

D'' is selected from the group of $-\text{H}$, alkyl, $-\text{OR}^2$, $-\text{OH}$, and $-\text{OC}(\text{O})\text{R}^3$;

each W^3 is independently selected from the group of $-\text{H}$, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

with the proviso that:

i) V , Z , W , W' are not all $-\text{H}$ and V^2 , Z^2 , W^2 , W'' are not all $-\text{H}$; and

R^2 is selected from R^3 and $-\text{H}$;

R^3 is selected from alkyl, aryl, alicyclic, and aralkyl;

each R^4 is independently selected from the group of $-\text{H}$, alkylene, -alkylenearyl and aryl, or together R^4 and R^4 are connected via 2-6 atoms, optionally including one heteroatom selected from the group of O, N, and S;

R^6 is selected from $-\text{H}$, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

n is an integer from 1 to 3;

R^{18} is independently selected from H, lower alkyl, aryl, and aralkyl, or, together, R^{12} and R^{18} are connected via 1-4 carbon atoms to form a cyclic group;

each R^{12} and each R^{13} is independently selected from H, lower alkyl, lower aryl, lower aralkyl, all optionally substituted, or R^{12} and R^{13} , together, are connected via 2-6 carbon atoms, optionally including 1 heteroatom selected from the group of O, N, and S, to form a cyclic group;

each R^{14} is independently selected from $-\text{OR}^{17}$, $-\text{N}(\text{R}^{17})_2$, $-\text{NHR}^{17}$, $-\text{SR}^{17}$, and $-\text{NR}^2\text{R}^{20}$;

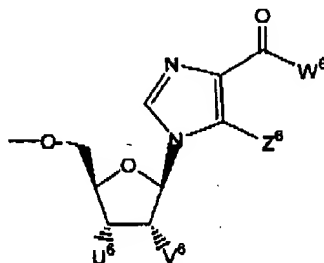
R^{15} is selected from -H, lower alkyl, lower aryl, and lower aralkyl, or, together, R^{15} and R^{16} are connected via 2-6 atoms to form a cyclic group, wherein the cyclic group optionally includes one heteroatom selected from O, N, and S;

R^{16} is selected from $-(CR^{12}R^{13})_n-C(O)-R^{14}$, -H, lower alkyl, lower aryl, and lower aralkyl, or, together, R^{15} and R^{16} are connected via 2-6 atoms to form a cyclic group, wherein the cyclic group optionally includes one heteroatom selected from O, N, and S;

each R^{17} is independently selected from lower alkyl, lower aryl, and lower aralkyl, or, when R^{14} is $-N(R^{17})_2$, together, both R^{17} s are connected via 2-6 atoms to form a cyclic group, wherein the cyclic group optionally includes one heteroatom selected from O, N, and S;

R^{20} is selected from the group of -H, lower R^3 , and $-C(O)$ -lower R^3 ; and

M is selected from the group consisting of

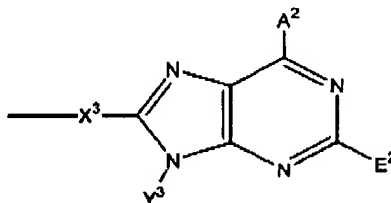


wherein:

U^6 and V^6 are independently selected from hydrogen, hydroxy, and acyloxy, or, when taken together, U^6 and V^6 form a lower cyclic ring containing at least one oxygen;

W^6 is selected from amino and lower alkyl amino; and

Z^6 is selected from alkyl and halogen;



and

wherein:

A^2 is selected from $-NR^8_2$, $-NHSO_2R^3$, $-OR^{25}$, $-SR^{25}$, halogen, lower alkyl, $-CON(R^4)_2$, guanidine, amidine, $-H$, and perhaloalkyl;

E^2 is selected from $-H$, halogen, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, $-CN$, and $-NR^7_2$;

X^3 is selected from $-alkyl(hydroxy)-$; $-alkyl-$; $-alkynyl-$; $-aryl-$; $-carbonyl-alkyl-$; $-1,1-dihaloalkyl-$; $-alkoxyalkyl-$; $-alkyloxy-$; $-alkylthioalkyl-$; $-alkylthio-$; $-alkylaminocarbonyl-$; $-alkylcarbonylamino-$; $-alicyclic-$; $-aralkyl-$; $-alkylaryl-$; $-alkoxycarbonyl-$; $-carbonyloxyalkyl-$; $-alkoxycarbonylamino-$; and $-alkylaminocarbonylamino-$, all optionally substituted, with the proviso that X^3 is not substituted with $-COOR^2$, $-SO_3H$, or $-PO_3R^2_2$;

Y^3 is selected from $-H$, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-R^{11}$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all, except H , optionally substituted;

each R^4 is independently selected from $-H$ and alkyl, or, together, both R^4 's form a cyclic alkyl group;

R^{25} is selected from lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

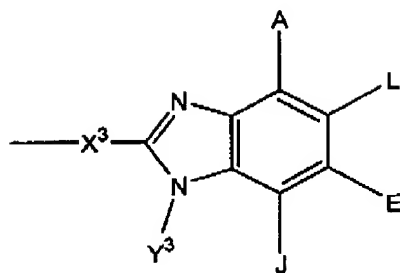
each R^7 is independently selected from $-H$, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

each R^8 is independently selected from $-H$, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or, together, both R^8 's form a bidentate alkyl;

R^{10} is selected from $-H$, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl; and

R^{11} is selected from alkyl, aryl, $-NR^2_2$, and $-OR^2$;

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and

wherein:

A, E, and L are independently selected from $-NR^8_2$, $-NO_2$, $-H$, $-OR^7$, $-SR^7$, $-C(O)NR_2$, halo, $-COR^{11}$, $-SO_2R^3$, guanidine, amidine, $-NHSO_2R^{25}$, $-SO_2NR^4_2$, $-CN$, sulfoxide, perhaloacyl, perhaloalkyl, perhaloalkoxy, C_1-C_5 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, and lower alicyclic, or, together, A and L form a cyclic group, or, together, L and E form a cyclic group, or, together, E and J form a cyclic group selected from the group of aryl, cyclic alkyl, and heterocyclic;

J is selected from $-NR^8_2$, $-NO_2$, $-H$, $-OR^7$, $-SR^7$, $-C(O)NR^4_2$, halo,

$-C(O)R^{11}$, $-CN$, sulfonyl, sulfoxide, perhaloalkyl, hydroxyalkyl, perhaloalkoxy, alkyl, haloalkyl, aminoalkyl, alkenyl, alkynyl, alicyclic, aryl, and aralkyl, or, together, J and Y form a cyclic group selected from the group of aryl, cyclic alkyl, and heterocyclic alkyl;

X^3 is selected from -alkyl(hydroxy)-; -alkyl-; -alkynyl-; -aryl-; -carbonyl-alkyl-; -1,1-dihaloalkyl-; -alkoxyalkyl-; -alkyloxy-; -alkylthioalkyl-; -alkylthio-; -alkylaminocarbonyl-; -alkylcarbonylamino-; -alicyclic-; -aralkyl-; -alkylaryl-; -alkoxycarbonyl-; -carbonyloxyalkyl-; -alkoxycarbonylamino-; and -alkylaminocarbonylamino-, all optionally substituted, with the proviso that X^3 is not substituted with $-COOR^2$, $-SO_3H$, or $-PO_3R^{22}_2$;

Y^3 is selected from $-H$, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-R^{11}$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted;

each R^4 is independently selected from $-H$ and alkyl, or, together, both R^4 s form a cyclic alkyl group;

R^{25} is selected from lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

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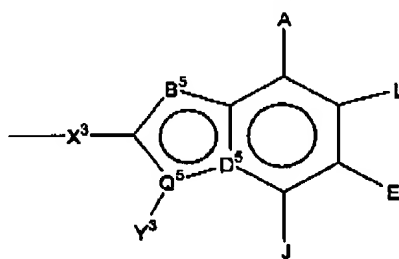
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each R^7 is independently selected from -H, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

each R^8 is independently selected from -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or, together, both R^8 's form a bidentate alkyl;

R^{10} is selected from -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl; and

R^{11} is selected from alkyl, aryl, $-NR^2_2$, and $-OR^2$;



and

wherein:

B^5 is selected from -NH-, -N= and $-CH=$;

D^5 is selected from $\begin{array}{c} | \\ -C= \end{array}$ and $\begin{array}{c} | \\ -N- \end{array}$;

Q^5 is selected from $-C=$ and $-N-$;

with the provisos that:

when B^5 is -NH-, Q^5 is $-C=$ and D^5 is $\begin{array}{c} | \\ -C= \end{array}$;

when B^5 is $-CH=$, Q^5 is $-N-$ and D^5 is $\begin{array}{c} | \\ -C= \end{array}$; and

when B^5 is $-N=$, D^5 is $\begin{array}{c} | \\ -N- \end{array}$ and Q^5 is $-C=$;

A, E, and L are independently selected from $-NR^8_2$, $-NO_2$, -H, $-OR^7$, $-SR^7$, $-C(O)NR^4_2$, halo, $-COR^{11}$, $-SO_2R^3$, guanidine, amidine, $-NHSO_2R^{25}$, $-SO_2NR^4_2$, -CN, sulfoxide, perhaloacyl, perhaloalkyl, perhaloalkoxy, C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, and lower alicyclic, or, together, A and L form a cyclic group, or, together, L and E form a cyclic group, or, together, E and J form a cyclic group selected from the group of aryl, cyclic alkyl, and heterocyclic;

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Y is selected from $-NR^8_2$, $-NO_2$, $-H$, $-OR^7$, $-SR^7$, $-C(O)NR^4_2$, halo, $-C(O)R^{11}$, $-CN$, sulfonyl, sulfoxide, perhaloalkyl, hydroxyalkyl, perhaloalkoxy, alkyl, haloalkyl, aminoalkyl, alkenyl, alkynyl, alicyclic, aryl, and aralkyl, or together with Y forms a cyclic group selected from the group of aryl, cyclic alkyl and heterocyclic alkyl;

X^3 is selected from -alkyl(hydroxy)-, -alkyl-, -alkynyl-, -aryl-, -carbonyl-alkyl-, -1,1-dihaloalkyl-, -alkoxyalkyl-, -alkyloxy-, -alkylthioalkyl-, -alkylthio-, -alkylaminocarbonyl-, -alkylcarbonylamino-, -alicyclic-, -aralkyl-, -alkylaryl-, -alkoxycarbonyl-, -carbonyloxyalkyl-, -alkoxycarbonylamino-, and -alkylaminocarbonylamino-, all optionally substituted; with the proviso that X^3 is not substituted with $-COOR^2$, $-SO_3H$, or $-PO_3R^2_2$;

Y^3 is selected from $-H$, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-R^{11}$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted;

R^4 is independently selected from $-H$ and alkyl, or together R^4 and R^4 form a cyclic alkyl group;

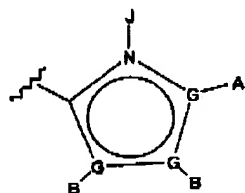
R^{25} is selected from lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

R^7 is independently selected from $-H$, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

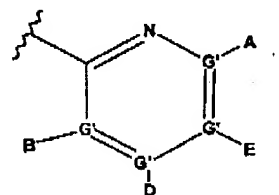
R^8 is independently selected from $-H$, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together they form a bidentate alkyl;

R^{10} is selected from $-H$, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from alkyl, aryl, $-NR^2_2$ and $-OR^3$;



and



and

wherein:

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each G is independently selected from C, N, O, S, and Se, and wherein not more than one G is O, S, or Se, and not more than one G is N;

each G' is independently selected from C and N and wherein no more than two G' groups are N;

A is selected from -H, -NR⁴₂, -CONR⁴₂, -CO₂R³, halo, -S(O)R³, -SO₂R³, alkyl, alkenyl, alkynyl, perhaloalkyl, haloalkyl, aryl, -CH₂OH, -CH₂NR⁴₂, -CH₂CN, -CN, -C(S)NH₂, -OR³, -SR³, -N₃, -NHC(S)NR⁴₂, -NHAc, and null;

each B and D are independently selected from -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, alkoxyalkyl, -C(O)R¹¹, -C(O)SR³, -SO₂R¹¹, -S(O)R³, -CN, -NR⁹₂, -OR³, -SR³, perhaloalkyl, halo, -NO₂, and null, all except -H, -CN, perhaloalkyl, -NO₂, and halo are optionally substituted;

E is selected from -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, alkoxyalkyl, -C(O)OR³, -CONR⁴₂, -CN, -NR⁹₂, -NO₂, -OR³, -SR³, perhaloalkyl, halo, and null, all except -H, -CN, perhaloalkyl, and halo are optionally substituted;

J is selected from -H and null;

X is an optionally substituted linking group that links R⁵ to the phosphorus atom via 2-4 atoms, including 0-1 heteroatoms selected from N, O, and S, except that if X is urea or carbamate there are 2 heteroatoms, measured by the shortest path between R⁵ and the phosphorus atom, and wherein the atom attached to the phosphorus is a carbon atom, and wherein X is selected from furan-2,5-diyl, -alkyl(hydroxy)-, -alkynyl-, -heteroaryl-, -carbonylalkyl-, -1,1-dihaloalkyl-, -alkoxyalkyl-, -alkyloxy-, -alkylthioalkyl-, -alkyl-, -thio-, -alkylaminocarbonyl-, -alkylcarbonylamino-, -alkoxycarbonyl-, -carbonyloxyalkyl-, -alkoxycarbonylamino-, and -alkylaminocarbonylamino-, all optionally substituted; with the proviso that X is not substituted with -COOR², -SO₃H, or -PO₃R²₂;

R² is selected from R³ and -H;

R³ is selected from alkyl, aryl, alicyclic, and aralkyl;

each R⁴ is independently selected from -H, and alkyl, or together R⁴ and R⁴ form a cyclic alkyl group;

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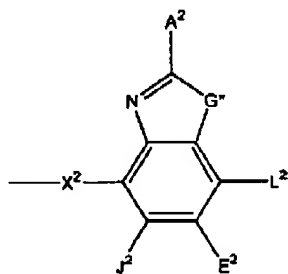
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each R^9 is independently selected from -H, alkyl, aralkyl, and alicyclic, or together R^9 and R^9 form a cyclic alkyl group or a heterocyclic group where the heteroatom is selected from the group of O, S and N;

R^{11} is selected from alkyl, aryl, $-NR^2$, and $-OR^2$;

and with the proviso that:

- 1) when G' is N, then the respective A, B, D, or E is null;
- 2) at least one of A and B, or A, B, D, and E is not selected from -H or null;
- 3) when R^5 is a six-membered ring, then X is not any 2 atom linker, an optionally substituted -alkyloxy-, or an optionally substituted -alkylthio-;
- 4) when G is N, then the respective A or B is not halogen or a group directly bonded to G via a heteroatom;
- 5) when X is not an -aryl- group, then R^5 is not substituted with two or more aryl groups;



and

wherein:

G'' is selected from -O- and -S-;

A^2 , L^2 , E^2 , and J^2 are selected from $-NR^4$, $-NO_2$, -H, $-OR^2$, $-SR^2$, $-C(O)NR^4$, halo, $-COR^{11}$, $-SO_2R^3$, guanidiny, amidiny, aryl, aralkyl, alkoxyalkyl, $-SCN$, $-NH SO_2R^9$, $-SO_2NR^4$, $-CN$, $-S(O)R^3$, perhaloacyl, perhaloalkyl, perhaloalkoxy, C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, and lower alicyclic, or together L^2 and E^2 or E^2 and J^2 form an annulated cyclic group;

X^2 is selected from $-CR^2_2$, $-CF_2$, $-CR^2_2-O-$, $-CR^2_2-S-$, $-C(O)-O-$, $-C(O)-S-$, $-C(S)-O-$, and $-CR^2_2-NR^{19}$, and wherein in the atom attached to the phosphorus is a carbon atom; with the proviso that X^2 is not substituted with $-COOR^2$, $-SO_3H$, or $-PO_3R^2$;

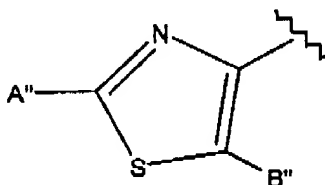
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2-114 (Canceled).

115 (New). The pharmaceutical composition according to claim 1, wherein M is

 A'' is of -H, $-NR^4_2$, $-CONR^4_2$, $-CO_2R^3$, halo, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 perhaloalkyl, C_1 - C_6 haloalkyl, aryl, $-CH_2OH$, $-CH_2NR^4_2$, $-CH_2CN$, -CN, $-C(S)NH_2$, $-OR^3$, $-SR^3$, $-N_3$, $-NHC(S)NR^4_2$, and $-NHAc$; B'' is -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, alkoxyalkyl, $-C(O)R^{11}$, $-C(O)SR^3$, $-SO_2R^{11}$, $-S(O)R^3$, -CN, $-NR^9_2$, $-OR^3$, $-SR^3$, perhaloalkyl, and halo, all except -H, -CN, perhaloalkyl, and halo are optionally substituted; X is selected from the group consisting of methylenoxycarbonyl and furan-2,5-diyl; YR^1 is OH or Y is NR^6 , wherein R^6 is selected from H, lower alkyl, acyclooxyalkyl, alkoxyalkyl, or lower acyl; and R^1 is independently selected from the group consisting of -H, $-[C(R^2)_2]_q-COOR^3$, $-C(R^4)_2COOR^3$, $-[C(R^2)_2]_q-C(O)SR^3$, and $-cycloalkylene-COOR^3$, wherein R^4 is, independently, alkyl or H and R_3 is alkyl, aryl, alicyclic or aralkyl.

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116 (New). The pharmaceutical composition of claim 115, wherein A" is -NH₂, -Cl, -Br, or -CH₃; B" is -H, -C(O)OR³, -C(O)SR³, C₁-C₆ alkyl, C(O)R¹¹, alicyclic, halo, heteroaryl, or -SR³ and all except -H, and halo are optionally substituted.

117 (New). The pharmaceutical composition of claim 116, wherein A" is -NH₂; B" is a C₁-C₆ alkyl or C(O)R¹¹, wherein R¹¹ is alkyl.

118 (New). The pharmaceutical composition of claim 115, wherein X is furan-2,5-diyl.

119 (New). The pharmaceutical composition of claim 1, wherein when Y is NR⁶, R⁶ is selected from H, lower alkyl, acyclooxyalkyl, alkoxycarbonylalkyl, or lower acyl; and R¹ is independently selected from the group consisting of -H, -[C(R²)₂]_q-COOR³, -C(R⁴)₂COOR³, -[C(R²)₂]_q-C(O)SR³, and -cycloalkylene-COOR³, wherein R⁴ is, independently, alkyl or H and R₃ is alkyl, aryl, alicyclic or aralkyl.

120 (New). The pharmaceutical composition of claim 119, wherein Y is NR⁶ and R⁶ is H; and R₁ is -C(R⁴)₂COOR³, wherein R⁴ is, independently, H or methyl; and R³ is alkyl.

121 (New). The pharmaceutical composition of claim 115, wherein A" is -NH₂; B" is a C¹-C⁶ alkyl or C(O)R¹¹, wherein R¹¹ is alkyl; and X is selected from the group consisting of methylenoxycarbonyl and furan-2,5-diyl.

122 (New). The pharmaceutical composition of claim 121, wherein X is furan-2,5-diyl.

123 (Withdrawn-New). The pharmaceutical composition of claim 115, wherein A" is -NH₂; B" is a C₁-C₆ alkyl or C(O)R¹¹, wherein R¹¹ is alkyl; and YR₁ is OH.

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124 (New). The pharmaceutical composition of claim 115, wherein A'' is -NH₂; B'' is a C1-C6 alkyl or C(O)R¹¹, wherein R¹¹ is alkyl; Y is NR⁶ and R⁶ is H; and R1 is -C(R⁴)₂COOR³, wherein R⁴ is, independently, H or methyl; and R³ is alkyl.

125 (Withdrawn-New). The pharmaceutical composition of claim 1, wherein X is furan-2,5-diyl and YR¹ is OH.

126 (New). The pharmaceutical composition of claim 1, wherein X is furan-2,5-diyl; Y is NR⁶ and R⁶ is H; and R1 is -C(R⁴)₂COOR³, wherein R⁴ is, independently, H or methyl; and R³ is alkyl.

127 (Withdrawn-New). The pharmaceutical composition of claim 115, wherein A'' is -NH₂; B'' is a C1-C6 alkyl or C(O)R¹¹, wherein R¹¹ is alkyl; X is selected from the group consisting of methylenoxycarbonyl and furan-2,5-diyl; and YR¹ is OH.

128 (Withdrawn-New). The pharmaceutical composition of claim 127, wherein X is furan-2,5-diyl.

129 (New). The pharmaceutical composition of claim 115, wherein A'' is -NH₂; B'' is a C1-C6 alkyl or C(O)R¹¹, wherein R¹¹ is alkyl; X is selected from the group consisting of methylenoxycarbonyl and furan-2,5-diyl; Y is NR⁶ and R⁶ is H; and R1 is -C(R⁴)₂COOR³, wherein R⁴ is, independently, H or methyl; and R³ is alkyl.

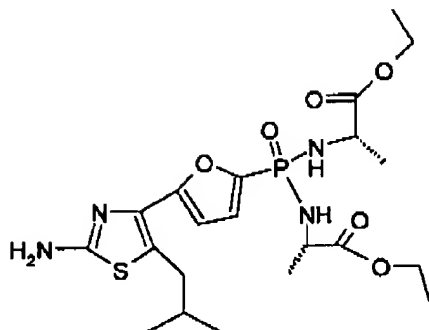
130 (New). The pharmaceutical composition of claim 129, wherein X is furan - 2, 5 - diyl.

131 (new). The pharmaceutical composition according to claim 1, wherein said FB Pase inhibitor is

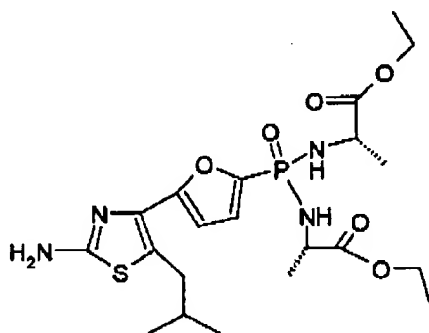
Compound J

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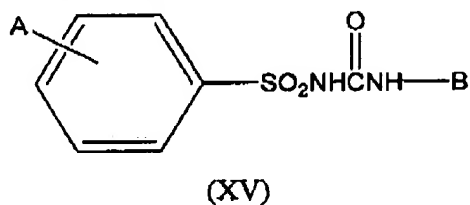
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132 (New). The pharmaceutical composition according to claim 1, wherein said sulfonylurea antidiabetic agent is glyburide and said FBPase inhibitor is Compound J



133. (New) The pharmaceutical composition of claim 1, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:



wherein

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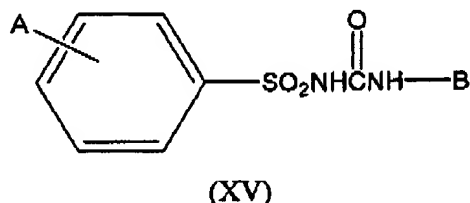
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A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;
and

B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

134. (New) The pharmaceutical composition of claim 133, wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

135. (New) The pharmaceutical composition of claim 131, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:



wherein

A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;
and

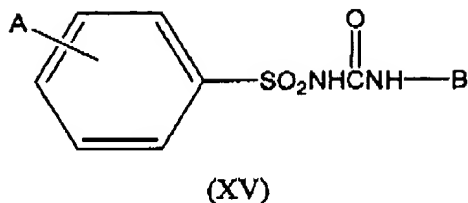
B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

136. (New) The pharmaceutical composition of claim 135, wherein said sulfonylurea antidiabetic agent is selected from glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

137. (New) The pharmaceutical composition of claim 129, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:

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wherein

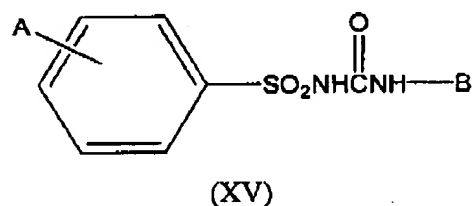
A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;

and

B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

138. (New) The pharmaceutical composition of claim 137, wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

139. (New) The pharmaceutical composition of claim 130, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:



wherein

A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;

and

B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

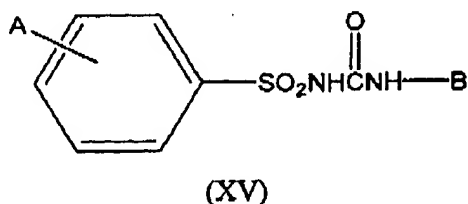
140. (New) The pharmaceutical composition of claim 139, wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide,

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glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

141. (Withdrawn-New) The pharmaceutical composition of claim 127, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:



wherein

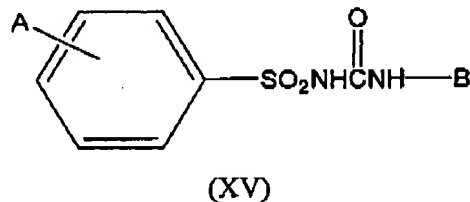
A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;

and

B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

142. (Withdrawn-New) The pharmaceutical composition of claim 141, wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

143. (Withdrawn-New) The pharmaceutical composition of claim 128, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:



wherein

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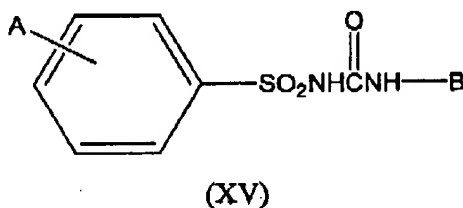
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A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;
and

B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

144. (Withdrawn-New) The pharmaceutical composition of claim 143, wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

145. (New) The pharmaceutical composition of claim 115, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:



wherein

A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;
and

B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

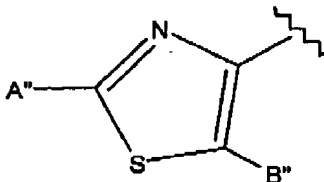
146. (New) The pharmaceutical composition of claim 145, wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

147. (New-Withdrawn) A method of treating an animal having diabetes comprising the administration of a composition according to claim 1 to an animal.

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148 (Withdrawn-New). The method of claim 147, wherein M of said FBPase inhibitor is



A'' is of -H, -NR⁴₂, -CONR⁴₂, -CO₂R³, halo, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ perhaloalkyl, C₁-C₆ haloalkyl, aryl, -CH₂OH, -CH₂NR⁴₂, -CH₂CN, -CN, -C(S)NH₂, -OR³, -SR³, -N₃, -NHC(S)NR⁴₂, and -NHAc;

B'' is -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, alkoxyalkyl, -C(O)R¹¹, -C(O)SR³, -SO₂R¹¹, -S(O)R³, -CN, -NR⁹₂, -OR³, -SR³, perhaloalkyl, and halo, all except -H, -CN, perhaloalkyl, and halo are optionally substituted;

X is selected from the group consisting of methylenoxycarbonyl and furan-2,5-diyl;

YR¹ is OH or Y is NR⁶, wherein R⁶ is selected from H, lower alkyl, acyclooxyalkyl, alkoxyalkyl, or lower acyl; and R¹ is independently selected from the group consisting of -H, -[C(R²)₂]_q-COOR³, -C(R⁴)₂COOR³, -[C(R²)₂]_q-C(O)SR³, and -cycloalkylene-COOR³, wherein R⁴ is, independently, alkyl or H and R₃ is alkyl, aryl, alicyclic or aralkyl.

149 (Withdrawn-New). The method of claim 148, wherein A'' is -NH₂, -Cl, -Br, or -CH₃; B'' is -H, -C(O)OR³, -C(O)SR³, C₁-C₆ alkyl, C(O)R¹¹, alicyclic, halo, heteroaryl, or -SR³ and all except -H, and halo are optionally substituted.

150 (Withdrawn-New). The method of claim 149, wherein A'' is -NH₂; B'' is a C₁-C₆ alkyl or C(O)R¹¹, wherein R¹¹ is alkyl.

151 (Withdrawn-New). The method of claim 148, wherein X is furan-2,5-diyl.

152 (Withdrawn-New). The method of claim 147, wherein when Y is NR⁶, R⁶ is selected from H, lower alkyl, acyclooxyalkyl, alkoxyalkyl, or lower acyl; and R¹ is

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independently selected from the group consisting of -H, $-[C(R^2)_2]_q-COOR^3$, $-C(R^4)_2COOR^3$, $-[C(R^2)_2]_q-C(O)SR^3$, and -cycloalkylene- $COOR^3$, wherein R^4 is, independently, alkyl or H and R_3 is alkyl, aryl, alicyclic or aralkyl.

153 (Withdrawn-New). The method of claim 152, wherein Y is NR^6 and R^6 is H; and R_1 is $-C(R^4)_2COOR^3$, wherein R^4 is, independently, H or methyl; and R^3 is alkyl.

154 (Withdrawn-New). The method of claim 148, wherein A'' is $-NH_2$; B'' is a C^1-C^6 alkyl or $C(O)R^{11}$, wherein R^{11} is alkyl; and X is selected from the group consisting of methylenoxycarbonyl and furan-2,5-diyl.

155 (Withdrawn-New). The method of claim 154, wherein X is furan-2,5-diyl.

156 (Withdrawn-New). The method of claim 148, wherein A'' is $-NH_2$; B'' is a C^1-C^6 alkyl or $C(O)R^{11}$, wherein R^{11} is alkyl; and YR^1 is OH.

157 (Withdrawn-New). The method of claim 148, wherein A'' is $-NH_2$; B'' is a C^1-C^6 alkyl or $C(O)R^{11}$, wherein R^{11} is alkyl; Y is NR^6 and R^6 is H; and R_1 is $-C(R^4)_2COOR^3$, wherein R^4 is, independently, H or methyl; and R^3 is alkyl.

158 (Withdrawn-New). The method of claim 147, wherein X of said FB Pase inhibitor is furan-2,5-diyl and YR^1 is OH.

159 (Withdrawn-New). The method of claim 147, wherein X of said FB Pase inhibitor is furan-2,5-diyl; Y is NR^6 and R^6 is H; and R_1 is $-C(R^4)_2COOR^3$, wherein R^4 is, independently, H or methyl; and R^3 is alkyl.

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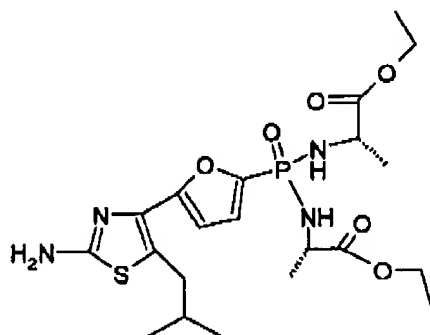
160 (Withdrawn-New). The method of claim 148, wherein A" is -NH_2 ; B" is a C1-C6 alkyl or C(O)R^{11} , wherein R^{11} is alkyl; X is selected from the group consisting of methylenoxycarbonyl and furan-2,5-diyl; and YR^1 is OH.

161 (Withdrawn-New). The method of claim 160, wherein X is furan-2,5-diyl.

162 (Withdrawn-New). The method of claim 148, wherein A" is -NH_2 ; B" is a C1-C6 alkyl or C(O)R^{11} , wherein R^{11} is alkyl; X is selected from the group consisting of methylenoxycarbonyl and furan-2,5-diyl; Y is NR^6 and R^6 is H; and R1 is $\text{-C(R}^4)_2\text{COOR}^3$, wherein R^4 is, independently, H or methyl; and R^3 is alkyl.

163 (Withdrawn-New). The method of claim 162, wherein X is furan - 2, 5 - diyl.

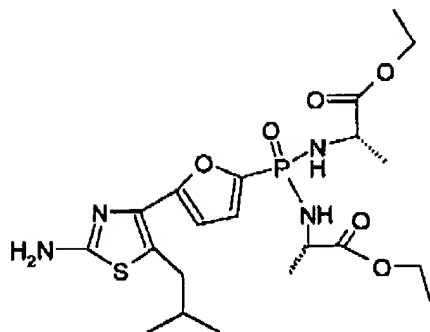
164 (Withdrawn-New). The method of claim 147, wherein said FBPase inhibitor is Compound J



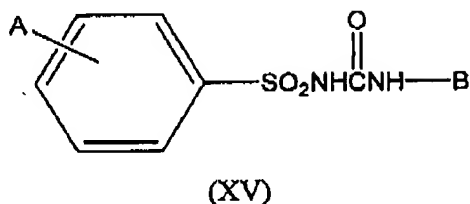
165 (Withdrawn-New). The method of claim 147, wherein said sulfonylurea antidiabetic agent is glyburide and said FBPase inhibitor is Compound J

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166. (Withdrawn-New) The method of claim 147, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:



wherein

A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;

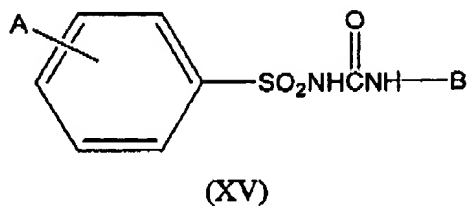
and

B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

167. (Withdrawn-New) The method of claim 166, wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

168. (Withdrawn-New) The method of claim 164, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:

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wherein

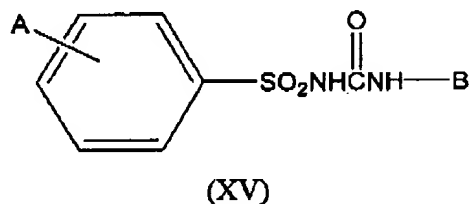
A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;

and

B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

169. (Withdrawn-New) The method of claim 168, wherein said sulfonylurea antidiabetic agent is selected from glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

170. (Withdrawn-New) The method of claim 162, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:



wherein

A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;

and

B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

171. (Withdrawn-New) The method of claim 170, wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide,

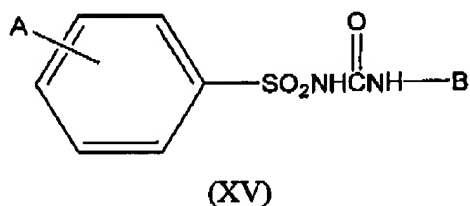
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glibornuride, tolbutamide, tolazamide, glipizide, glyclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

172. (Withdrawn-New) The method of claim 163, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:



wherein

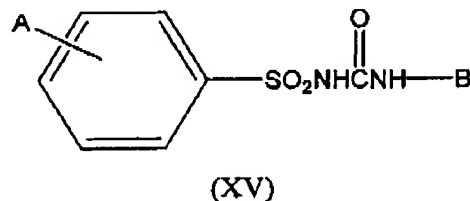
A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;

and

B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

173. (Withdrawn-New) The method of claim 172, wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, glyclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

174. (Withdrawn-New) The method of claim 160, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:



wherein

A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;

and

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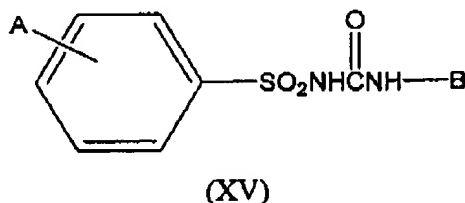
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B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

175. (Withdrawn-New) The method of claim 174, wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

176. (Withdrawn-New) The method of claim 161, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:



wherein

A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;

and

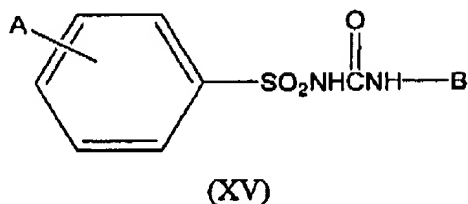
B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

177. (Withdrawn-New) The method of claim 176, wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

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178. (Withdrawn-New) The method of claim 147, wherein said sulfonylurea antidiabetic agent is a compound of formula XV:



wherein

A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl;

and

B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

179. (Withdrawn-New) The method of claim 178, wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.